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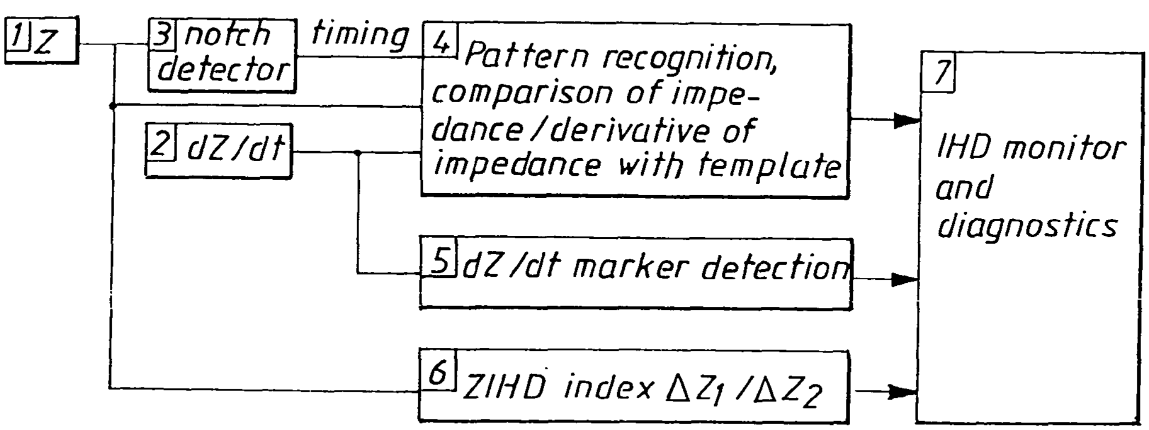
(54) **Apparatus for early detection of Ischemic Heart Disease**

(57) A monitor for early detection of an ischemic heart disease of a patient comprises an impedance measurement means (1) including electrode means for measuring an intracardiac impedance and generating a corresponding impedance signal. A notch detector (3) is connected to the impedance measurement means for detecting the occurrence of a notch in the impedance signal coincident with the entry of blood into the ventricle. A pattern recognition means (4) is provided to compare the measured post-notch impedance curve with a stored predetermined reference impedance curve template to detect an ischemic heart disease from the result of the comparison.

Fig. 5



EP 1 384 433 A1

Description

Technical Field

[0001] The present invention relates to a monitor for early detection of an ischemic heart disease of a patient comprising an impedance measurement means including electrode means for measuring an intracardiac impedance and generating a corresponding impedance signal, and a notch detector connected to said impedance measurement means detecting the occurrence of a notch in said impedance signal coincident with the entry of blood into the ventricle.

Background

[0002] A monitor of the above defined kind is described in WO 02/43587.

[0003] Congestive heart failure (CHF) is a fast growing health problem that mostly affects only adults. In this condition the heart is unable to pump enough blood to meet the need of the body's organs. Among the most common causes of CHF can be mentioned coronary artery disease, causing myocardial ischemia, myocardial infarction and cardiomyopathy. During ischemia the cardiac relaxation, i.e. diastolic, is changed or disturbed because the cardiac muscle is stiffened. A disturbed diastolic phase or diastolic failure is a very early kind of congestive heart failure, such that at this early state it might not even appear as symptoms to the patient. Detection of these early signs of disturbed relaxation patterns is described in the above mentioned WO 02/43587.

[0004] Early detection of ischemic heart disease (IHD) is required since that will give opportunities to prevent life threatening complications. By using a parameter such as diastolic intracardiac impedance IHD will be detected at a much earlier stage and myocardiac consequences such myocardial infarction (MI) and CHF may be prevented.

[0005] IHD prevents normal cardiac function because oxygen supply to the cardiac muscle is too low. In the acute stage of global cardiac ischemia (after 1-2s), relaxation failure occurs in the diastole (filling phase) as the myocardial tissue stiffens from lack of oxygen, followed by contraction failure (after 10s), increased filling pressures (after 20s), changes in ECG (after 25 s) and angina (30 s). Even if global ischemia is removed after a few seconds and oxygen supply is fully recovered, the disturbed relaxation may remain for hours or days. The diastole portion of the cardiac cycle seems to be the most sensitive parameter for IHD since it is effected first and residue effects remain for a long period after oxygen supply is restored. Cardiac tissue stiffness caused by IHD prevents adequate passive ventricular filling. The heart will try to compensate for this decreased filling by a largely increased atrial contraction. The atrial contribution to the ventricular filling in relation to passive filling will thus increase and this is often seen as an inverted Early filling/Atrial contribution (E/A) quotient in echocardiographical measurements of mitral blood flow. Figure 1 shows schematically the early filling E and the atrial contribution A of mitral value blood flow for a normal healthy heart and an abnormal heart suffering from IHD.

[0006] When IHD progresses it may lead to MI, CHF and/or the patient's death. In fact early detection of IHD can serve as an early marker for CHF risk factor.

[0007] Detection of the start of the diastolic phase by a "notch" detection is described in the above mentioned PCT/SE01/02615, cf. also Brian R. Pickett et. al., The American Journal of Cardiology, Vol. 71, May 1, 1993, " Usefulness of the Impedance Cardiogram to Reflect Left Ventricular Diastolic Function ", which describes a study of the correlation between a dip in a non-invasively measured impedance and Doppler measurements for diastolic studies showing the appearance of a notch in the impedance signal corresponding to early diastole of a cardiac cycle.

[0008] The intracardiac impedance reflects the blood volume in the heart chambers, and the purpose of the present invention is to provide a monitor for early detection of an ischemic heart decease as described above by studying the measured intracardiac impedance curve during a selected portion of the cardiac cycle related to said notch.

Disclosure of the invention

[0009] This purpose is obtained by a monitor of the type defined in the introductory portion of the description and having the characterizing features of claim 1.

[0010] The above discussed increased stiffness of the heart tissue caused by IHD is reflected in the shape of the post notch portion of the measured impedance curve and this phenomena is thus utilized in the monitor according to the invention for early detection of a ischemic heart decease.

[0011] Generally the impedance curve has a plateau after the notch, which for IHD patients is followed by a dominating decrease coinciding with atrial contraction, indicating that the atria of these IHD patients are trying to compensate for the reduced passive ventricular filling. To detect this decrease, according to an advantageous embodiment of the monitor according to the invention, a differentiating means is provided to calculate the time derivative, dZ/dt, of the impedance curve, and the pattern of recognition means is adapted to compare the shape of the time derivative in the post notch portion of the impedance curve with a predetermined reference impedance derivative template.

[0012] According to other advantageous embodiments of the monitor according to the invention a calculation means is provided to calculate, for each cardiac cycle, an ischemic heart decease index, ZIHD-index, defined by

$$\text{ZIHD-index} = \Delta Z_1/\Delta Z_2$$

where ΔZ_1 denotes, for each cardiac cycle, the difference between a maximum value of the measured impedance and the impedance value measured in a plateau occurring in the impedance curve after the notch, and ΔZ_2 the difference between the impedance value in the plateau and a minimum value of the measured impedance in an impedance decrease following the plateau, for detecting an ischemic heart disease from the calculated ZIHD-index. The ZIHD-index indicates the ratio between the passive filling and the contribution from the atrium to the ventricle filling. With the ZIHD-index the progression and degree of IHD can be monitored and the degree of cardiac compensation for the IHD can be calculated. The more the atrium is compensating for reduced passive ventricular filling the more advanced is the IHD. Atrial compensation is feasible only to a certain point and the more IHD progresses the more enlarged the atrium will become and the risk of atrial defibrillation AF is increased. By monitoring the ZIHD-index development of AF problems can be avoided. Alternatively to the monitoring of the ZIHD-index a first comparison means can be provided to compare the absolute value $|\Delta Z_1|$ of ΔZ_1 and/or the absolute value $|\Delta Z_2|$ of ΔZ_2 with a predetermine ΔZ_1 threshold value and/or a predetermined ΔZ_2 threshold value respectively. ΔZ_2 is a measure of the function of the atrium and by monitoring ΔZ_2 it is possible to observe how the disease is advancing.

[0013] The post-notch plateau is not always a horizontal plateau and some patients have an overshoot after the notch. It is therefore advantageous, according to still another embodiment of the monitor according to the invention, to provide a first averaging means to determine an average value of the measured impedance curve in a predetermined time window after the notch for use as a plateau impedance value. The delay of said window after the notch is selectable and the length of the time window is preferably in the range of 100-150 msec.

[0014] According to yet other advantageous embodiments of the monitor according to the invention a loop creator is connected to the impedance measurement means and to the differentiating means to receive the impedance signal and the first time derivative dZ/dt of the impedance signal for plotting impedance values against related time derivative values to form a loop for each cardiac cycle, and a third comparison means is connected to the loop creator for comparing the loop with a predetermined loop template to detect an ischemic heart disease from the result of the comparison. The third comparison means is preferably adapted to compare the shape of the loop in that part of the loop, which corresponds to the post-notch portion of the impedance curve, with corresponding part of the loop template. By analyzing such a loop very clear indications can be obtained of deviations indicating an ischemic heart disease.

[0015] According to still other advantageous embodiments of the monitor according to the invention a second averaging means is connected to the impedance measuring means for determining an average impedance signal of impedance signals measured during a predetermined number of cardiac cycles, and the pattern recognition means is connected to the second averaging means to compare the average value of the post-notch impedance curves with the reference impedance curve template. A third averaging means can be connected to the differentiating means for determining an average time derivative of impedance signals measured during a predetermined number of cardiac cycles, and the pattern recognition means is connected to the third averaging means to compare the average time derivative of the post-notch portion of the measured impedance curves with corresponding part of the reference impedance derivative template. The loop creator is preferably connected to the second and third averaging means to receive the averaging impedance signal and average time derivative to form a corresponding average loop, and the third comparison means is adapted to compare the average loop with the predetermined loop template. By using average quantities in this way in the detection of an ischemic heart disease the reliability in the detection can be still improved.

Brief description of the drawings

[0016] To explain the invention in greater details an exemplifying embodiment of the monitor according to the invention with the described with reference to figure 5 on the drawings, on which figure 1 illustrates the ratio between the early passive filling and the atrial contribution to the mitral valve blood flow for a normal heart and an abnormal heart suffering from an ischemic heart disease, figure 2 shows results of impedance measurements formed in a humans heart, figure 3 shows average value and standard deviation for a plurality of impedance measurements, figure 4 illustrates use of the first time derivative of the impedance curve for detection of an ischemic heart disease, and figure 5 shows in the form of the block diagram an embodiment chosen as an example of the monitor according to the invention.

Description of a preferred embodiment

[0017] Figure 2 shows results of right ventricular impedance measurements in four humans, viz. A) a 73 year old male, suffering from IHD and having a normal ejection fraction EF of 70% (patient number 14), B) a 67 year old male, suffering from IHD and having a reduced EF of 35% (patient number 6), C) a 24 year old male, having no IHD and reduced EF of 42% (patient number 20), and D) a healthy 27 year old female (patient number 19).

[0018] AC impedance measurements were performed using measuring catheters of type USCI Baid EP. Current was injected between a tip electrode positioned in right ventricular apex and a ring separated 10 mm from the tip. The resulting voltage response was measured between the same two electrodes.

[0019] In figure 2 the average value and the standard deviation for the measured impedance Z, the corresponding quantities for the first time derivative of the impedance curves dZ/dt, as well as a normalized ECG as a function of time.

[0020] These measurements can be used to discriminate IHD from non-IHD by using pattern recognition by comparing the post-notch impedance curve or its time derivative to "normal" impedance templates or "normal" first time derivative templates.

[0021] From figure 2 appears that for humans suffering from IHD the measured impedance curve Z exhibits, after the notch indicated in the figure by a vertical dashed bold line, a plateau followed by the steep decrease. The impedance curve Z for a non-IHD human has no such plateau and decrease, cf. diagrams C) and D) in figure 2.

[0022] In the corresponding dZ/dt curves IHD manifests itself as a distinct minimum in the post-notch region, encircled in diagram A) and B) in figure 2. Such a distinct minimum cannot be traced in the dZ/dt curves from non-IHD humans.

[0023] The measured Z and dZ/dt curves can be used for creating loops as described in the above mentioned PCT/SE01/02615 and IHD be detected by analyzing that part of the resulting loops which correspond to the post-notch portion of the impedance curves.

[0024] Figure 3 shows the average impedance curve and the standard deviation from measurements on the plurality of cardiac cycles for A) a IHD patient and B) a healthy patient.

[0025] It appears from figure 3 that patients having IHD, independent of EF status, exhibit a plateau after the notch in the impedance curve Z followed by a dominating, distinct decrease coinciding with atrial contraction. The position of the notch is marked in the diagrams of figure 3 by a dashed, vertical, bold line. As discussed above this decrease corresponds to the compensation by the atrium for the reduced passive filling of the ventricle of these patients.

[0026] The impedance curve Z for non-IHD patients may also have a plateau like portion after the impedance notch and atrial contraction may also be seen as a decrease in the impedance curve, but not as clear and dominating as for IHD patients.

[0027] Discriminating IHD patients from non-IHD patients can be accomplished by calculating a ZIHD-index $= \Delta Z_1/\Delta Z_2$.

[0028] As appears from figure 3

$$\Delta Z_1 = Z_{max} - Z_{plateau}$$

where Z_{max} denotes the maximum value of the impedance curve in the notch region and $Z_{plateau}$ the impedance value of the post-notch plateau, and

$$\Delta Z_2 = Z_{plateu} - Z_{min}$$

where Z_{min} denotes minimum value in the decrease following the plateau.

[0029] This index ZIHD is smaller for IHD patients, diagram A), than for non-IHD patients, diagram B).

[0030] The maximum value Z_{max} appears in figure 3 before the notch, however sometimes a maximum value of the impedance after the notch can be used. For some patients it can be suitable to use as maximum value Z_{max} an average value of a maximum value occurring before the notch and a maximum value occurring after the notch, cf. figure 2A).

[0031] The plateau value $Z_{plateau}$ can preferably be determined as an average value of the measured impedance curve in a predetermined time window after the notch. The length of this window can suitably be in the range of 100-150 msec and the location of the time window can be delayed more or less after the notch depending on the appearance of the impedance curve in the vicinity of the notch (occurrence of possible overshoots, etc.). The time from the occurrence of the notch to the steep decrease in the measured Z curve is depending on the heart rate, the length of the plateau decreasing with increasing heart rate. This must also be taken into consideration when determining the length of the time window.

[0032] Figure 4 shows the dZ/dt curves and the normalized ECG:s of figure 2. From this figure it appears that by using a suitably selected discriminating threshold level, indicated by a horisontal dashed bold line after the notch in the dZ/dt-curves, the large down-slope coinciding with atrial activity for IHD patients can be correctly detected. Thus for humans A) and B) the dZ/dt curves decrease below the marked threshold value indicating IHD, whereas for humans C) and D) the dZ/dt curves never reach this threshold, indicating non-IHD.

[0033] Figure 5 shows a preferred embodiment of the monitor according to the invention in the form of a block diagram. The measured impedance Z, block 1, is supplied to a notch detector 3, of the kind described in PCT/SE01/02615. The notch detector 3 detects notch existence and timing in the measured impedance curve. The pattern recogniser 4 detects the shape of the post-notch impedance curve and compares it with a stored predetermined reference or normal impedance curve template.

[0034] A differentiating means is provided to calculate the first time derivative dZ/dt, block 2, which is also supplied to the pattern recogniser 4 for comparison of the shape of the dZ/dt curve in the post-notch portion with a predetermined reference impedance derivative template.

[0035] dZ/dt is also supplied to a dZ/dt marker detector 5 for detecting the large negative dZ/dt-values of IHD patients coinciding with atrial activity after detection of a notch as described above, eg. by comparing dZ/dt with a predetermined threshold value.

[0036] The ZIHD-index calculator 6 is calculating the ZIHD-index = $\Delta Z_1/\Delta Z_2$ for use for distinguishing IHD patients from non-IHD patients as described above. With the aid of the ZIHD-index the IHD progression or degree can be monitored. Progressing IHD results in increasing atrial compensation for reduced passive ventricular filling. However, this compensation is only possible to a certain point. With still progressing IHD the atrium will become enlarged and the risk of atrial defibrillation is obvious. By monitoring the ZIHD-index future atrial defibrillation problems can be avoided.

[0037] The embodiment shown in figure 5 also comprises a monitor and diagnostics unit 7 for collecting, analyzing and storing measuring data. Sometimes the notch does not appear clearly and might be difficult to detect. Information from previous measurements on the patient in question can in this case be used for locating the decrease in the impedance curve corresponding to atrial activity.

Claims

1. A monitor for early detection of an ischemic heart disease of a patient comprising an impedance measurement means (1) including electrode means for measuring an intracardiac impedance and generating a corresponding impedance signal, and a notch detector (3) connected to said impedance measurement means for detecting the occurrence of a notch in said impedance signal coincident with the entry of blood into the ventricle, **characterized in that** a pattern recognition means (4) is provided to compare the measured post-notch impedance curve with a stored predetermined reference impedance curve template to detect an ischemic heart disease from the result of the comparison.

2. The monitor according to claim 1, **characterized in that** said pattern recognition means (4) is adapted to compare the shape of the post-notch portion of the impedance curve with said impedance curve template.

3. The monitor according to claims 1 or 2, **characterized in that** a differentiating means (2) is provided to calculate the time derivative, dZ/dt, of the impedance curve, and **in that** said pattern recognition means (4, 5) is adapted to compare the shape of said time derivative in the post-notch portion of the impedance curve with a predetermined reference impedance derivative template.

4. The monitor according to any of the preceding claims, **characterized in that** a calculation means is provided to calculate, for each cardiac cycle, an ischemic heart disease index, ZIHD-index, defined by

$$\text{ZIHD-index} = \Delta Z_1/\Delta Z_2$$

where ΔZ_1 denotes, for each cardiac cycle, the difference between a maximum value of the measured impedance and the impedance value measured in a plateau occurring in the impedance curve after said notch, and ΔZ_2 the difference between the impedance value in said plateau and a minimum value of the measured impedance in an impedance decrease following said plateau, for detecting an ischemic heart disease from the calculated ZIHD-index.

5. The monitor according to the claim 4, **characterized in that** a first comparison means is provided to compare the absolute value $|\Delta Z_1|$ of ΔZ_1 and/or the absolute value $|\Delta Z_2|$ of ΔZ_2 with a predetermined ΔZ_1 threshold value and/or a predetermined ΔZ_2 threshold value respectively.

6. The monitor according to claims 4 or 5, **characterized in that** said maximum value of the measured impedance is a maximum value located before the notch in the cardiac cycle.

7. The monitor according to the claims 4 or 5, **characterized in that** said maximum value of the measured impedance is a maximum value located after the notch in the cardiac cycle.

8. The monitor according to the claims 4 or 5, **characterized in that** said maximum value of the measured impedance is an average value of a maximum value located before the notch in the cardiac cycle and a maximum value located after the notch.

9. The monitor according to any of the claims 4 - 8, **characterized in that** a first averaging means is provided to determine an average value of the measured impedance curve in a predetermined time window after the notch for use as a plateau impedance value.

10. The monitor according to the claim 9, **characterized in that** the delay of time window after the notch is selectable.

11. The monitor according to the claims 9 or 10, **characterized in that** the length of said time window is in the range of 100-150 msec.

12. The monitor according to any of the claims 3-11, **characterized in that** said differentiating means (2) is adapted to determine the slope of said impedance decrease following the plateau in the impedance curve from said time derivative, dZ/dt, of the impedance signal, and **in that** a second comparison means (5) is provided to compare said slope with a predetermined slope threshold level.

13. The monitor according to any of the claims 3 - 12, **characterized in that** a loop creator is connected to said impedance measurement means (1) and to said differentiating means (2) to receive said impedance signal and said first time derivative dZ/dt of the impedance signal for plotting impedance values against related time derivative values to form a loop for each cardiac cycle, and **in that** a third comparison means is connected to said loop creator for comparing said loop with a predetermined loop template to detect an ischemic heart disease from the result of the comparison.

14. The monitor according to claim 13, **characterized in that** said third comparison means is adapted to compare the shape of the loop **in that** part of the loop, which corresponds to the post-notch portion of the impedance curve, with corresponding part of said loop template.

15. The monitor according to any of the preceding claims, **characterized in that** a second averaging means is connected to said impedance measuring means (1) for determining an average impedance signal of impedance signals measured during a predetermined number of cardiac cycles, and **in that** said pattern recognition means (4) is connected to said second averaging means to compare the average value of the post-notch impedance curves with said reference impedance curve template.

16. The monitor according to any of the claims 3 - 15, **characterized in that** a third averaging means is connected to said differentiating means (2) for determining an average time derivative of impedance signals measured during a predetermined number of cardiac cycles, and **in that** said pattern recognition means is connected to said third averaging means to compare said average time derivative (4, 5) of the post-notch portion of the measured impedance curves with corresponding part of said reference impedance derivative template.

17. The monitor according to claims 15 and 16, **characterized in that** said loop creator is connected to said second and third averaging means to receive said average impedance signal and said average time derivative to form a corresponding average loop, and **in that** said third comparison means is adapted to compare said average loop with said predetermined loop template.

18. The monitor according to any of the claims 5 - 17, **characterized in that** said first, second and third comparison means are realised by one and the same comparison means.

19. The monitor according to any of the claims 9-18, **characterized in that** said first, second and third averaging means are realised by one and the same averaging means.

20. The monitor according to any of the preceding claims, **characterized in that** said electrode means comprises a bipolar ventricular electrode and **in that** said impedance measuring means (1) is adapted to measure the impedance between electrode tip and ring.

21. The monitor according to any of the claims 1 - 19, said monitor being implantable, **characterized in that** said electrode means comprises an unipolar ventricular electrode and **in that** said impedance measuring means (1) is adapted to measure the impedance between electrode and monitor casing.

22. A heart stimulator comprising a pulse generator for generating stimulation pulses for delivery to a patient's heart by means of electrode means adapted for location in one or both of the lower chambers of the heart, **characterized by** a monitor according to any one of the preceding claims.

Fig. 1

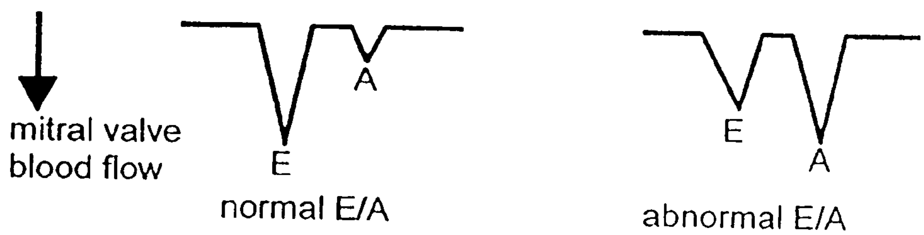

mitral valve
blood flow
A
E
normal E/A
E
A
abnormal E/A

Fig. 5

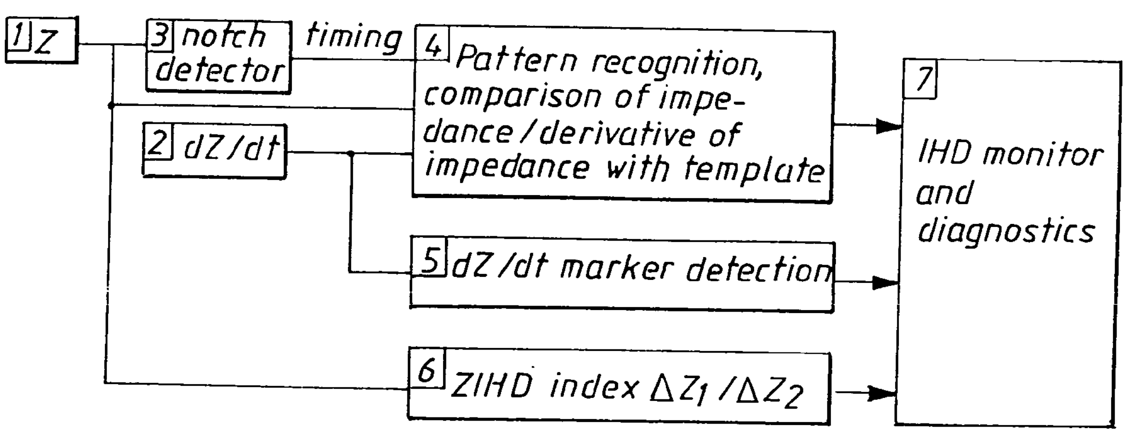
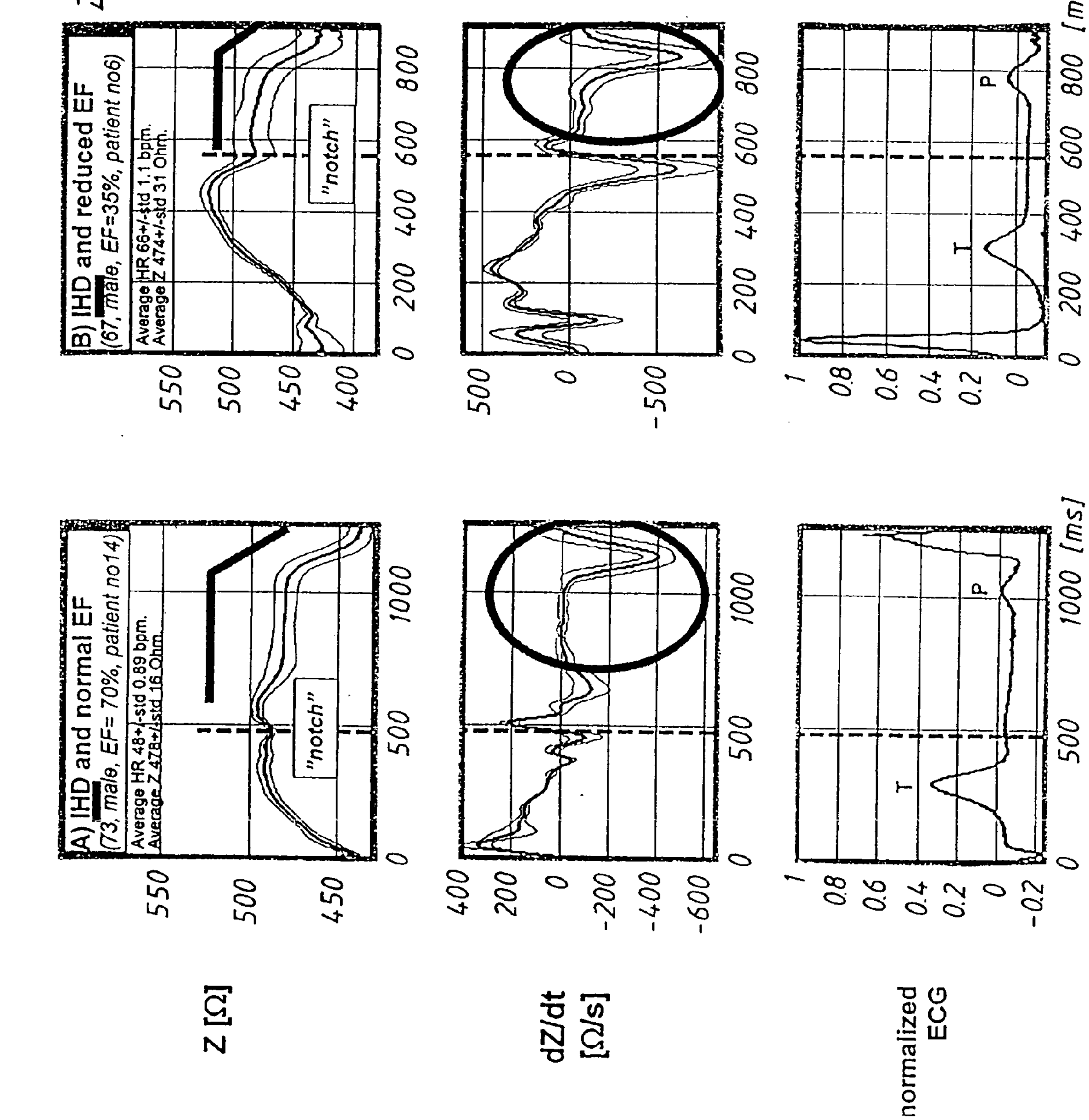

1 Z
3 notch detector
timing
4 Pattern recognition, comparison of impedance/derivative of impedance with template
2 dZ/dt
5 dZ/dt marker detection
6 ZIHD index ΔZ1/ΔZ2
7 IHD monitor and diagnostics

Fig. 2A,B


A) IHD and normal EF
(73, [redacted] male, EF= 70%, patient no14)
Average HR 48+/-std 0.89 bpm.
Average Z 478+/-std 16 Ohm.
"notch"
B) IHD and reduced EF
(67, [redacted] male, EF=35%, patient no6)
Average HR 66+/-std 1.1 bpm.
Average Z 474+/-std 31 Ohm.
"notch"
Z [Ω]
dZ/dt [Ω/s]
normalized ECG
T
P
[ms]
550
500
450
400
200
0
-200
-400
-600
-500
1
0.8
0.6
0.4
0.2
-0.2
1000
800
600

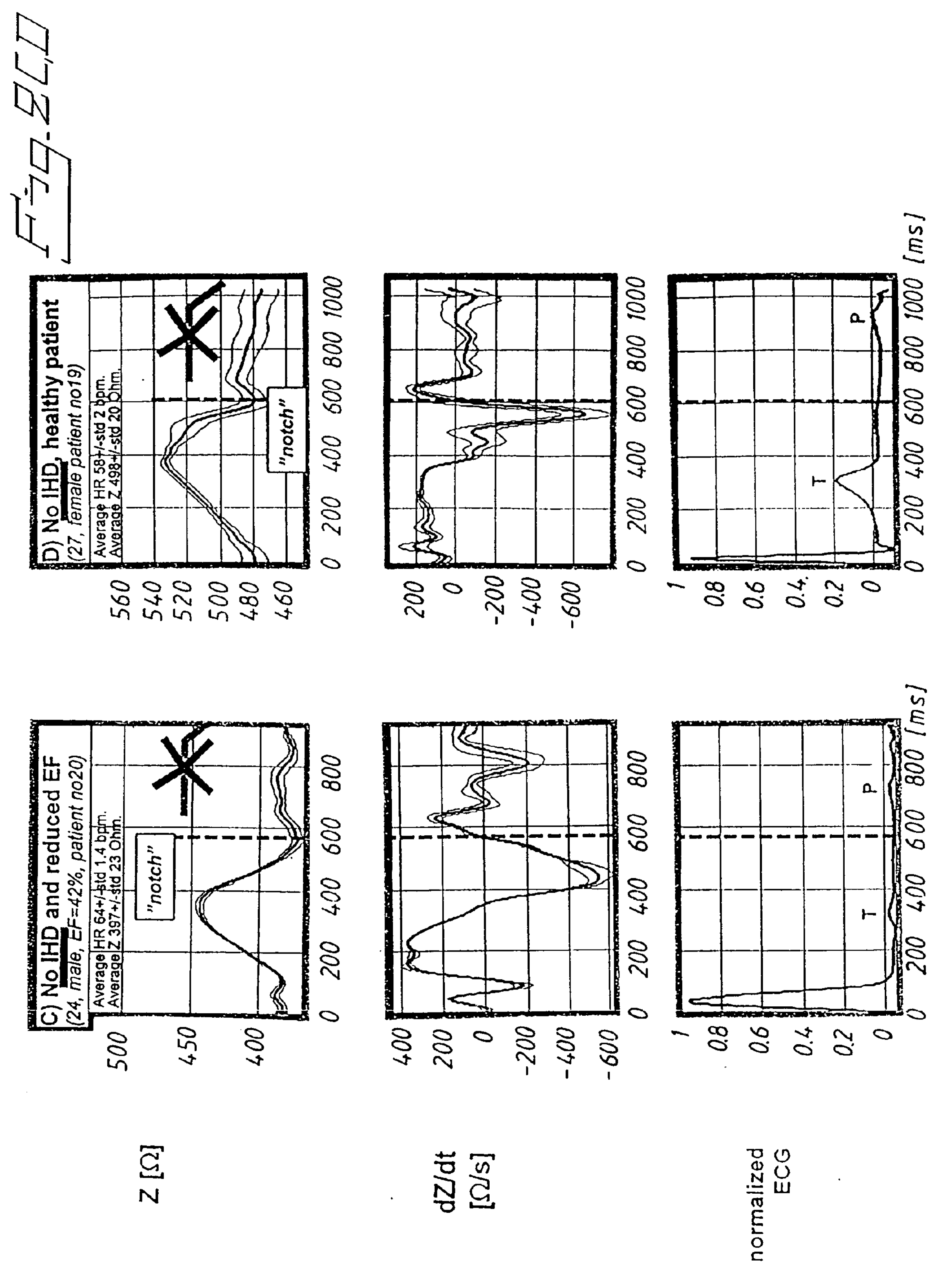


Fig. 2C,D
C) No IHD and reduced EF
(24, male, EF=42%, patient no20)
Average HR 64+/-std 1.4 bpm.
Average Z 397+/-std 23 Ohm.
"notch"
D) No IHD, healthy patient
(27, female patient no19)
Average HR 58+/-std 2 bpm.
Average Z 498+/-std 20 Ohm.
"notch"
Z [Ω]
dZ/dt [Ω/s]
normalized ECG
T
P
[ms]

Fig. 3 A) IHD patient

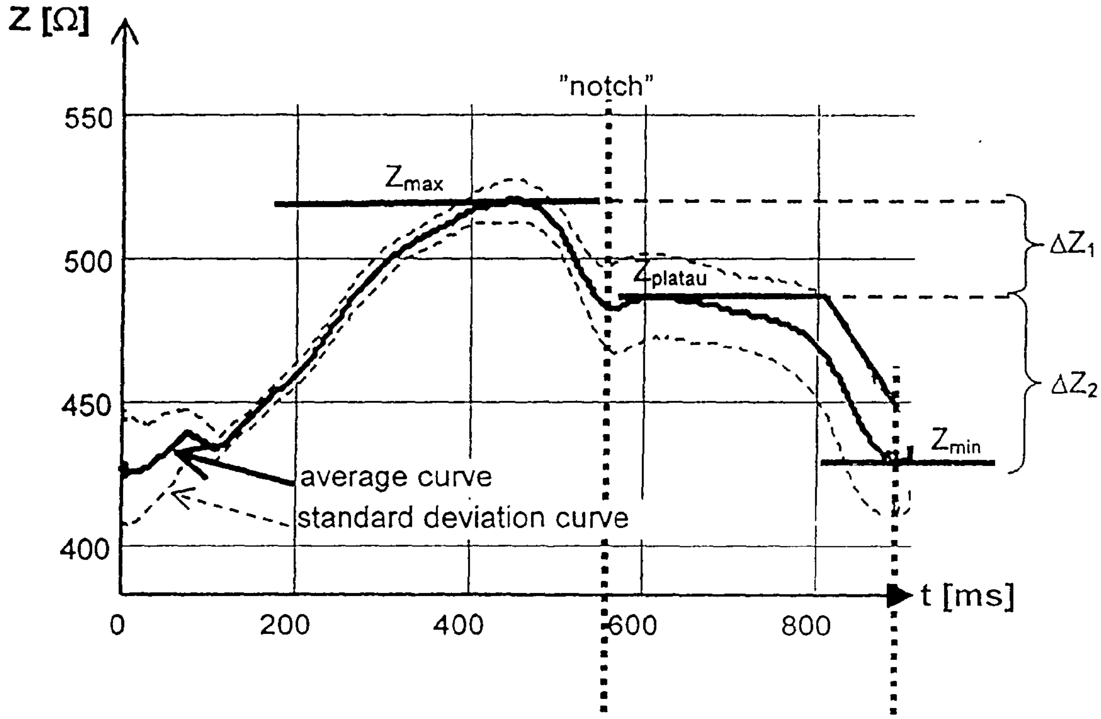
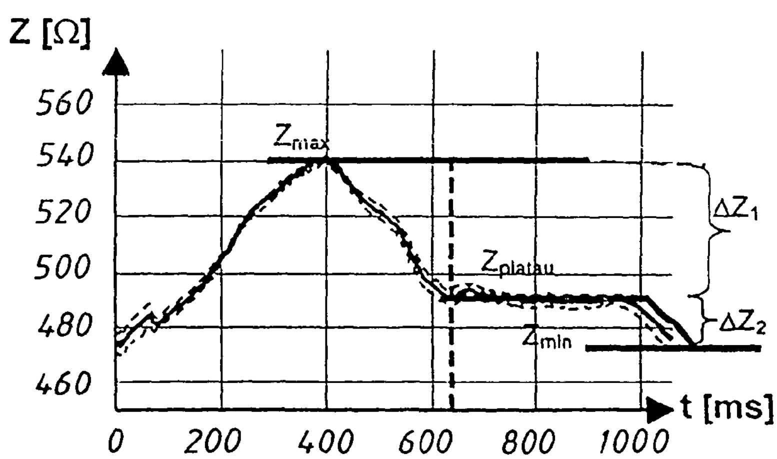


Fig. 3 B) Healthy patient



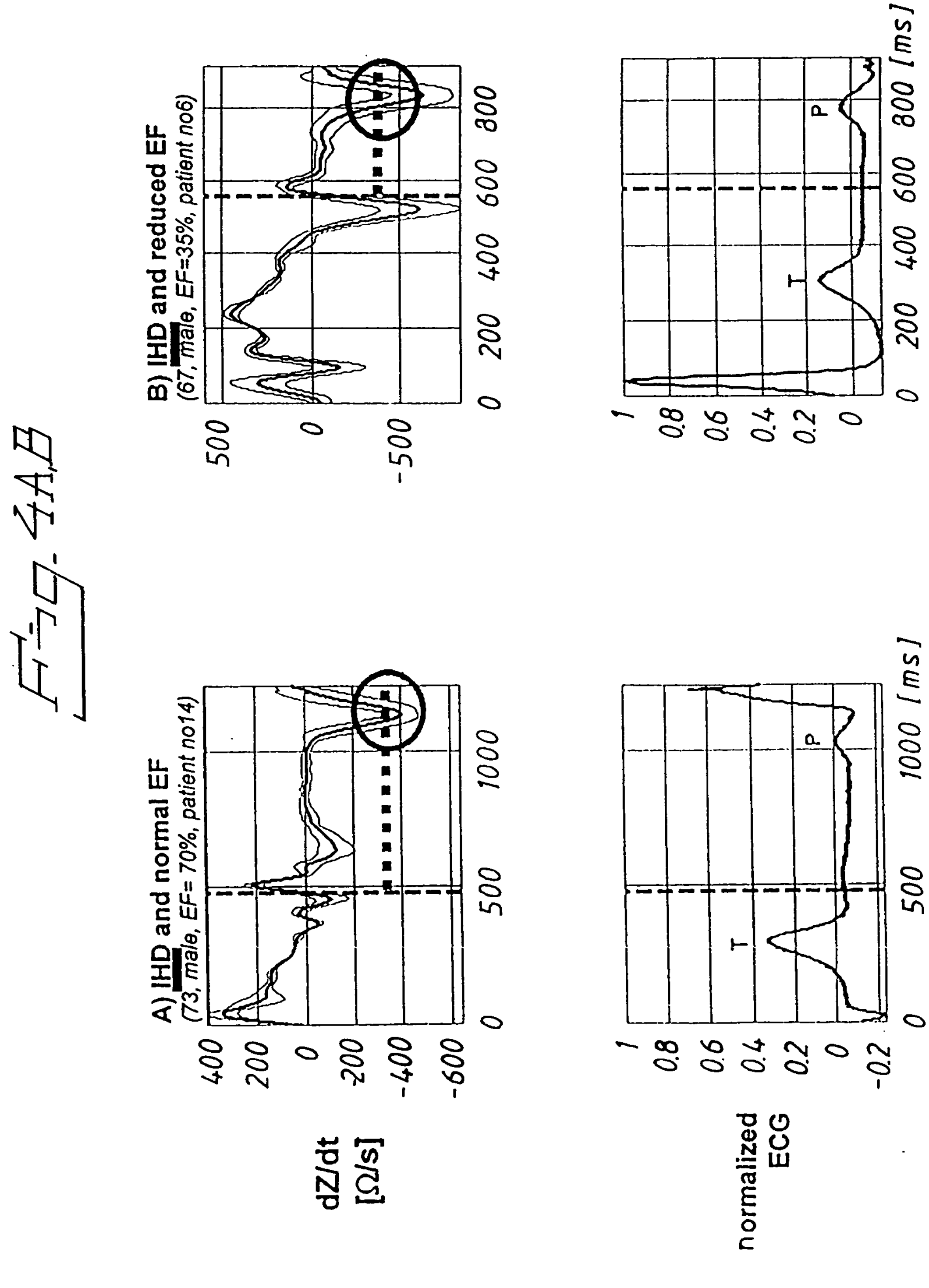
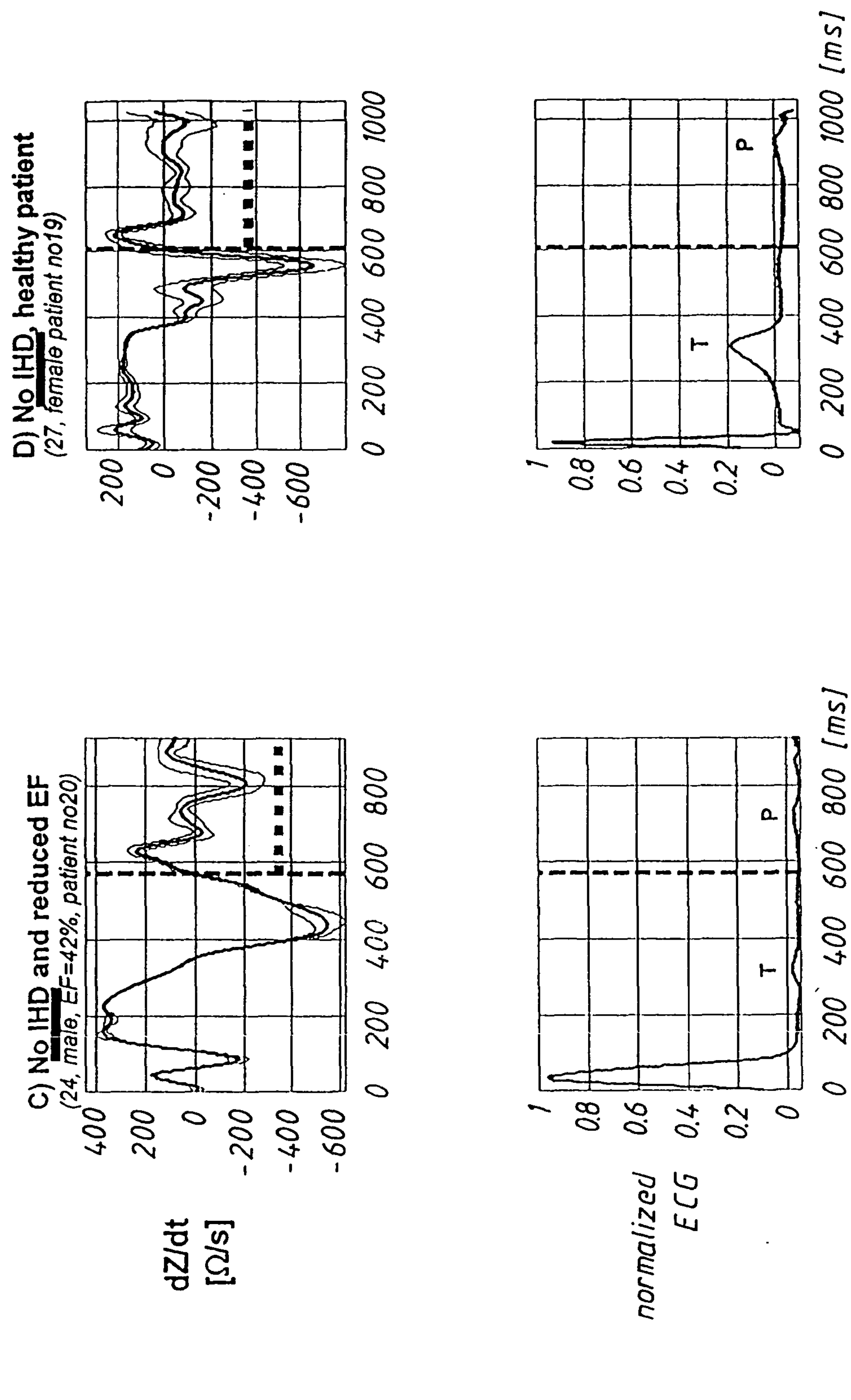

A) IHD and normal EF
(73, [redacted] male, EF= 70%, patient no14)
B) IHD and reduced EF
(67, [redacted] male, EF=35%, patient no6)
dZ/dt
[Ω/s]
normalized
ECG
400
200
0
-200
-400
-600
500
-500
1
0.8
0.6
0.4
0.2
-0.2
T
P
500
1000
200
400
600
800
[ms]

Fig. 4A,B

Fig. 4C, D


C) No IHD and reduced EF
(24, [redacted] male, EF=42%, patient no20)
D) No IHD, healthy patient
(27, [redacted] female patient no19)
dZ/dt
[Ω/s]
normalized
ECG
T
P
[ms]
0 200 400 600 800 1000
400 200 0 -200 -400 -600
1 0.8 0.6 0.4 0.2 0

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 03 01 2263

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y,D	WO 02 43587 A (JAERVERUD KARIN ;ST JUDE MEDICAL AB (SE)) 6 June 2002 (2002-06-06) * page 2, paragraph 1 * * page 3, paragraph 6 - page 4, paragraph 3 * ---	1,2	A61B5/00
Y,D	PICKETT B R ET AL: "USEFULNESS OF THE IMPEDANCE CARDIOGRAM TO REFLECT LEFT VENTRICULAR DIASTOLIC FUNCTION" AMERICAN JOURNAL OF CARDIOLOGY, CAHNERS PUBLISHING CO., NEWTON, MA,, US, vol. 71, May 1993 (1993-05), pages 1099-1103, XP001095143 ISSN: 0002-9149 * page 1, column 2, paragraph 2 * ---	1,2	
A	KUBICEK W G ET AL: "THE MINNESOTA IMPEDANCE CARDIOGRAPH - THEORY AND APPLICATIONS" BIOMEDICAL ENGINEERING, UNITED TRADE PRESS, LONDON,, GB, vol. 9, no. 9, September 1974 (1974-09), pages 410-416, XP001051054 ISSN: 0006-2898 * whole document * ---	1-21	TECHNICAL FIELDS SEARCHED (Int.Cl.7) A61N A61B
A	EP 0 607 511 B (SIEMENS ELEMA AB) 27 July 1994 (1994-07-27) * whole document * ---	1-21	
A	US 5 282 840 A (HUDRLIK TERRENCE R) 1 February 1994 (1994-02-01) * whole document * ---	1-21	
A	US 2002/002389 A1 (BRADLEY KERRY ET AL) 3 January 2002 (2002-01-03) * whole document * -----	1-21	

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	22 October 2003	Edward, V

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
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O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 03 01 2263

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